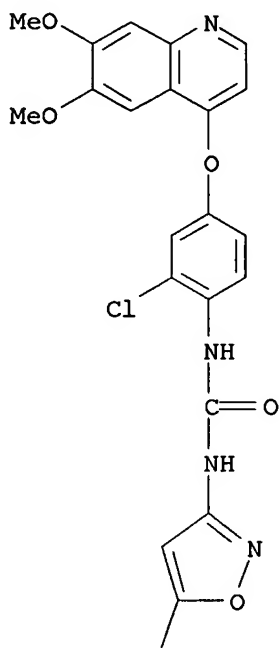


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 ED Entered STN: 04 Dec 2002
 CN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)- (9CI) (CA INDEX NAME)
 OTHER NAMES:
 CN N-[2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)urea
 FS 3D CONCORD
 MF C22 H19 Cl N4 O5
 CI COM
 SR CA
 LC STN Files: CA, CAPLUS, PROUSDDR, TOXCENTER, USPAT2, USPATFULL

PAGE 1-A



PAGE 2-A

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> FILE REG

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
68.70	84.91

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.75

FILE 'REGISTRY' ENTERED AT 15:55:56 ON 02 MAR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 1 MAR 2006 HIGHEST RN 875609-25-9
DICTIONARY FILE UPDATES: 1 MAR 2006 HIGHEST RN 875609-25-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=> STR 475108-18-0

:END

L5 STRUCTURE CREATED

=> S L5 FAM FUL

FULL SEARCH INITIATED 15:55:59 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 15 TO ITERATE

100.0% PROCESSED 15 ITERATIONS 12 ANSWERS
SEARCH TIME: 00.00.01

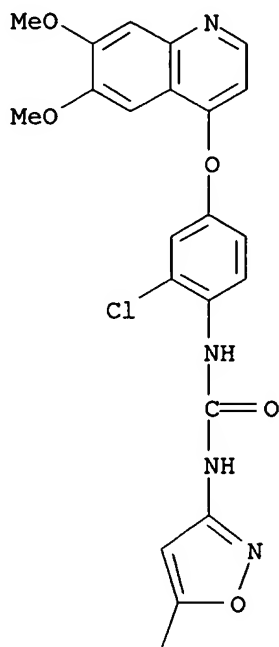
L6 12 SEA FAM FUL L5

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=> D SCAN

L6 12 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
 IN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)-, hydrate (9CI)
 MF C22 H19 Cl N4 O5 . x H2 O

PAGE 1-A



PAGE 2-A

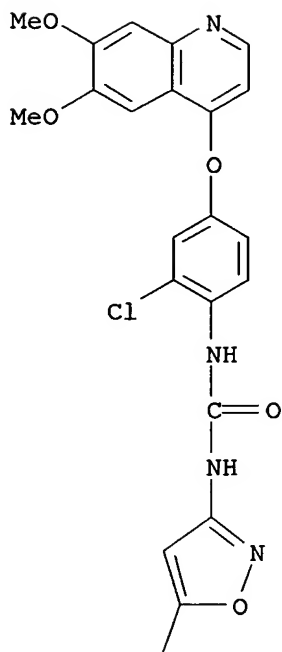
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● x H₂O

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

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L6 ANSWER 1 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN
 RN 682745-43-3 REGISTRY
 ED Entered STN: 18 May 2004
 CN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)-, monohydrochloride (9CI) (CA INDEX NAME)
 MF C22 H19 Cl N4 O5 . Cl H
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 CRN (475108-18-0)



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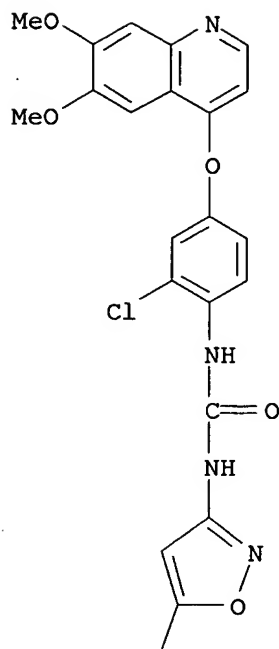
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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 2 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN
RN 682745-42-2 REGISTRY
ED Entered STN: 18 May 2004
CN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)-, mono(4-methylbenzenesulfonate), monohydrate (9CI) (CA INDEX NAME)
MF C22 H19 Cl N4 O5 . C7 H8 O3 S . H2 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

CM 1

CRN 475108-18-0
CMF C22 H19 Cl N4 O5

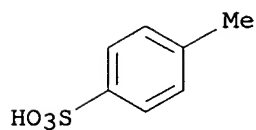


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CM 2

CRN 104-15-4

CMF C7 H8 O3 S



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RN 682745-41-1 REGISTRY

ED Entered STN: 18 May 2004

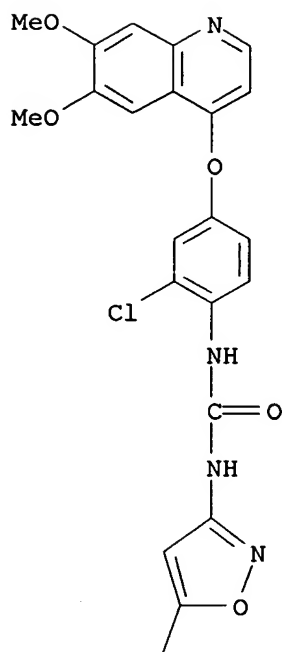
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SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

CRN (475108-18-0)



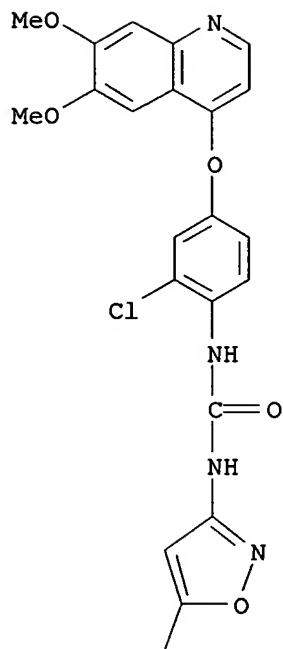
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● HCl

● H₂O

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ED Entered STN: 18 May 2004
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MF C22 H19 Cl N4 O5 . H2 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
CRN (475108-18-0)

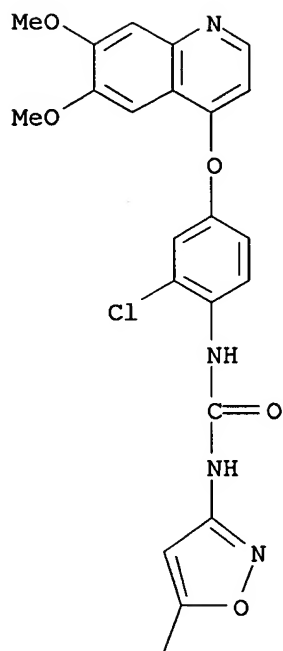


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● H₂O

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 5 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN
RN 682745-39-7 REGISTRY
ED Entered STN: 18 May 2004
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MF C22 H19 Cl N4 O5 . x H2 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
CRN (475108-18-0)



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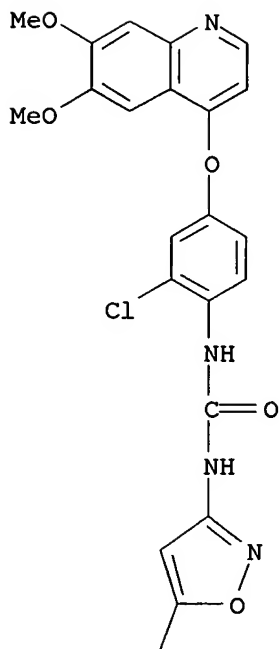
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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 6 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN
RN 682745-38-6 REGISTRY
ED Entered STN: 18 May 2004
CN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H19 Cl N4 O5 . x C4 H4 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

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CRN 475108-18-0
CMF C22 H19 Cl N4 O5



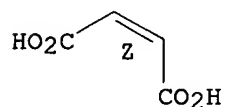
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CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 7 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN

RN 682745-37-5 REGISTRY

ED Entered STN: 18 May 2004

CN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)-, 4-methylbenzenesulfonate (9CI) (CA INDEX NAME)

MF C22 H19 Cl N4 O5 . x C7 H8 O3 S

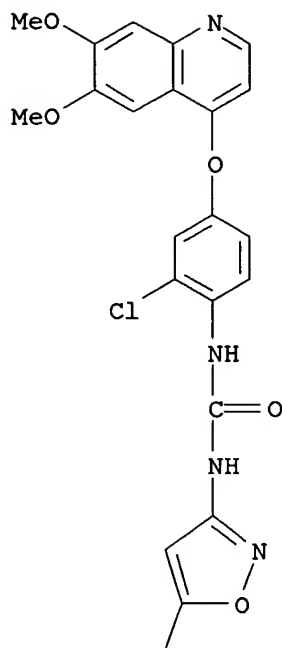
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CRN 475108-18-0
CMF C22 H19 Cl N4 O5

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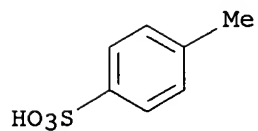


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CM 2

CRN 104-15-4
CMF C7 H8 O3 S



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L6 ANSWER 8 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN
RN 682745-36-4 REGISTRY
ED Entered STN: 18 May 2004
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MF C22 H19 Cl N4 O5 . x C H4 O3 S
SR CA

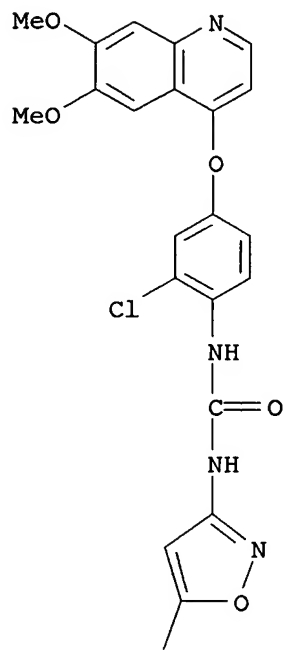
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CRN 475108-18-0

CMF C22 H19 Cl N4 O5

PAGE 1-A



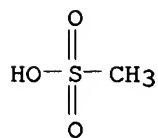
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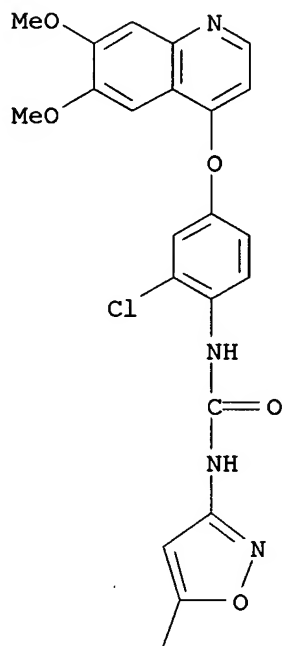
L6 ANSWER 9 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN
RN 682745-35-3 REGISTRY
ED Entered STN: 18 May 2004

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MF C22 H19 Cl N4 O5 . x H2 O4 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

CM 1

CRN 475108-18-0
CMF C22 H19 Cl N4 O5

PAGE 1-A

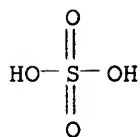


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CM 2

CRN 7664-93-9
CMF H2 O4 S



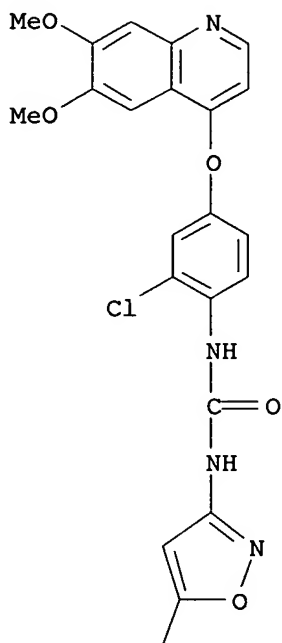
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L6 ANSWER 10 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN
 RN 682745-34-2 REGISTRY
 ED Entered STN: 18 May 2004
 CN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)-, nitrate (9CI) (CA INDEX NAME)
 MF C22 H19 Cl N4 O5 . x H N O3
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER

CM 1

CRN 475108-18-0
 CMF C22 H19 Cl N4 O5

PAGE 1-A

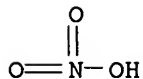


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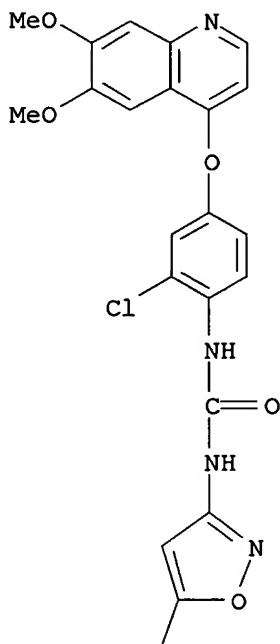
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L6 ANSWER 11 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN
RN 682745-33-1 REGISTRY
ED Entered STN: 18 May 2004
CN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)-, hydrochloride (9CI) (CA INDEX NAME)
MF C22 H19 Cl N4 O5 . x Cl H
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LC STN Files: CA, CAPLUS, TOXCENTER
CRN (475108-18-0)

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PAGE 2-A

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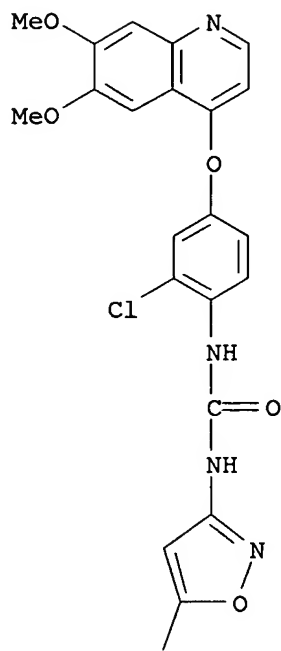
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ED Entered STN: 04 Dec 2002
CN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN N-[2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(5-methyl-3-

isoxazolyl)urea
FS 3D CONCORD
MF C22 H19 Cl N4 O5
CI COM
SR CA
LC STN Files: CA, CAPLUS, PROUSDDR, TOXCENTER, USPAT2, USPATFULL

PAGE 1-A



PAGE 2-A

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3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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L2 ANALYZE L1 1 RN : 34 TERMS

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L3 34 S L2
L4 1 S 475108-18-0

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L5 STR 475108-18-0
L6 12 S L5 FAM FUL

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L7 3 S L6

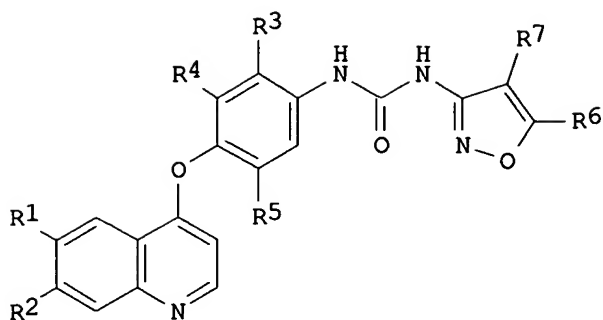
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L8 2 L7 NOT L1

=> d bib abs hitstr 1-2

L8 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:589418 CAPLUS
DN 141:117198
TI Therapeutic agent for wet age-related macular degeneration
IN Matsuno, Kiyoshi; Koyama, Shinji
PA Santen Pharmaceutical Co., Ltd., Japan; Kirin Beer Kabushiki Kaisha
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004060373	A1	20040722	WO 2003-JP16854	20031226
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	JP 2004217649	A2	20040805	JP 2003-431849	20031226
PRAI	JP 2002-379857	A	20021227		
GI					



I

AB A therapeutic agent for wet age-related macular degeneration which contains as an active ingredient an N-quinolyloxyphenyl-N'-isoxazolylurea derivative represented by the general formula (I; wherein R1 and R2 each is C1-6 alkoxy; R3 is halogeno; R4 and R5 each is hydrogen, halogeno, etc.; and R6 and R7 each is hydrogen, halogeno, C1-4 alkyl, etc.). The compound has excellent choroidal angiogenesis inhibitory activity and is useful in treatments for wet age-related macular degeneration.

IT **475108-18-0**, N-{2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-methyl-3-isoxazolyl)urea **475108-18-0D**, N-{2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-methyl-3-isoxazolyl)urea, salts

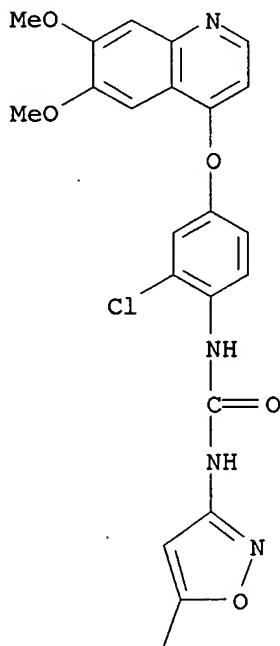
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(N-quinolyloxyphenyl-N'-isoxazolylurea derivs. as therapeutic agents for wet age-related macular degeneration)

RN 475108-18-0 CAPLUS

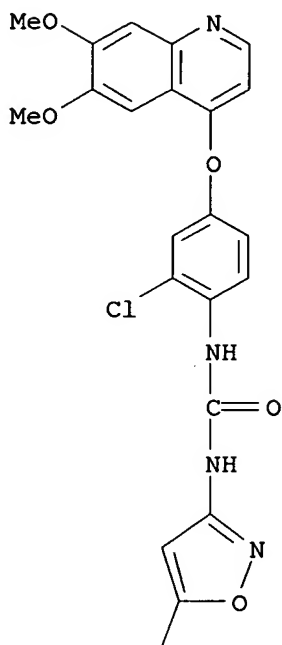
CN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)- (9CI) (CA INDEX NAME)

PAGE 1-A



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RN 475108-18-0 CAPLUS
 CN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)- (9CI) (CA INDEX NAME)



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Me

L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2002:849617 CAPLUS
 DN 137:370101
 TI Preparation of quinoline derivatives having azolyl group and quinazoline derivatives as antitumor agents
 IN Kubo, Kazuo; Sakai, Teruyuki; Nagao, Rika; Fujiwara, Yasunari; Isoe, Toshiyuki; Hasegawa, Kazumasa
 PA Kirin Beer Kabushiki Kaisha, Japan
 SO PCT Int. Appl., 89 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

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PI	WO 2002088110	A1	20021107	WO 2002-JP4279	20020426

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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JP 3602513	B2	20041215		
US 2003087907	A1	20030508	US 2002-132473	20020426
US 6821987	B2	20041123		
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ZA 2003007861	A	20041008	ZA 2003-7861	20031008
NO 2003004595	A	20031219	NO 2003-4595	20031014
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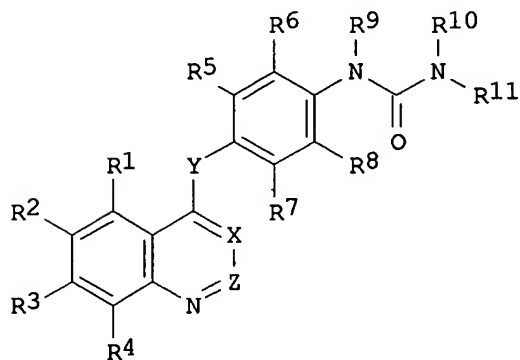
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US 2002-132473 A3 20020426

WO 2002-JP4279 W 20020426

OS MARPAT 137:370101

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AB N-[(4-quinolinyl or 4-quinazolinyl)thio or -oxy]phenyl-N'-azolylylurea derivs. represented by the formula (I) or pharmaceutically acceptable salts or solvates thereof [wherein X, Z = CH, N; Y = O, S; R1, R2, R3 = H, NO2, NH2, each (un)substituted C1-6 alkyl or alkoxy or C2-6 alkenyl or alkynyl; R4 = H; R5-R8 = H, halo, C1-4 alkyl, alkoxy, or alkylthio, CF3, NO2, NH2; R9, R10 = C1-6 alkyl, each (un)substituted C1-4 alkylcarbonyl or C1-6 alkyl; R11 = (un)substituted azolylyl] are prepared. These compds. are useful for the treatment of tumor, diabetic retinopathy, chronic articular rheumatism, psoriasis, atherosclerosis, and Kaposi's sarcoma. They are also used for inhibiting neovascularization of a target blood vessel by contacting them with vascular endothelial cells of the target blood

vessel. Thus, 100 mg 2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline was dissolved in 5 mL CHCl₃ and 0.5 mL Et₃N, treated with a solution of 100 mg triphosgene in CHCl₃, and stirred at room temperature for 15 min, followed by adding 49 mg 2-aminothiazole, and the resulting mixture was stirred at room temperature overnight to give 31 mg N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]-N'-(1,3-thiazol-2-yl)urea (II). II at 20 mg/kg/day for 9 days inhibited the growth of human lung cancer transplanted in nude mice by 92.0%. The compds. I in vitro showed IC₅₀ of 0.001-0.0697 μ M for inhibiting the phosphorylation of the intracellular domain of human vascular endothelial cell growth factor (VEGF) receptor KDR (kinase insert domain-containing receptor) in IH3T3 cell expressing human KDR.

IT 475108-18-0P, N-[2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)urea

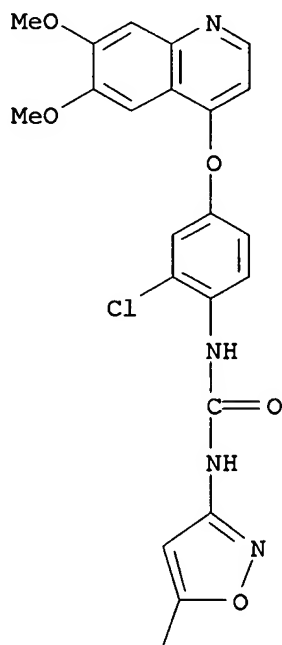
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-[(4-quinolinyl or 4-quinazolinyl)oxy]phenyl-N'-azolyurea derivs. as neovascularization inhibitors for treatment of tumor, diabetic retinopathy, chronic articular rheumatism, psoriasis, atherosclerosis, and Kaposi's sarcoma)

RN 475108-18-0 CAPLUS

CN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

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